



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,084	12/15/2003	Joseph C. Walsh	2003P88073 US	3273
28524 7590 11/14/2008 SIEMENS CORPORATION INTELLECTUAL PROPERTY DEPARTMENT 170 WOOD AVENUE SOUTH ISELIN, NJ 08830				
EXAMINER KRISHNAN, GANAPATHY				
ART UNIT		PAPER NUMBER		
1623				
MAIL DATE		DELIVERY MODE		
11/14/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/736,084

Applicant(s)

WALSH ET AL.

Examiner

Ganapathy Krishnan

Art Unit

1623

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 August 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7-14, 16-22 and 25-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-14, 16-22 and 25-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The amendment filed 8/11/2008 has been received, entered and carefully considered.

The following information provided in the amendment affects the instant application:

1. Claims 6, 15, 23-24 and 32-34 have been canceled.
2. Claims 1, 10, 12, 14, 16, 21 and 30 have been amended.
3. Remarks drawn to rejections under 35 USC 103 (a).
Claims 1-5, 7-14, 16-22 and 25-31 are pending in the case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection Claims 1-5, 7-14, 16-22 and 25-31 under 35 U.S.C. 103(a) as being unpatentable over Fox et al (The Journal of Organic Chemistry, 1968, 33(4), 1592-99) in view of Miller et al (J. Org. Chem. 1963, 28, 936-41) is being maintained for reasons of record.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicants have traversed the rejection arguing that:

1. Fox et al do not teach nor suggest the use of 2,3'-anhydrothymidine as the starting material as instantly claimed. Fox teaches 2,5'-anhydrothymidine as the starting material for compound 8 of his invention.

2. Miller discloses 2,3'-anhydrothymidine derivative but does not teach or suggest opening of the 2,3'-anhydrothymidine derivative to form an enolate. Fox does not suggest this either.

3. The 2,5'-anhydrothymidine of Fox has a 7-membered ring whereas the 2,3'-anhydrothymidine of the instant invention has a 6-membered ring. The stabilities of the two rings systems are different and in turn their reactivities will be different. Because of the unpredictable nature of chemical reactions one of skill in the art will have no reasonable expectation of success in replacing the 2,5'-anhydrothymidine derivative of Fox with the 2,3'-anhydrothymidine derivative to arrive at the claimed invention.

4. Fox and Miller do not suggest the use of alkoxide as instantly claimed. The conversion of compound 4 to compound 8 as in Fox may not be feasible in alkoxide since the mesylate at

the 3' position may also get cleaved. Compound 8 of Fox does not have a protected 5' hydroxyl. The 5'-position is protected before the ring opening reaction of the anhydrothymidine in the instant invention. In contrast the 5'-position need not be protected in Fox et al since it is forming a cyclic ring.

Applicants' arguments are not found to be persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988 and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

It is true that Fox teaches the use of 2,5'-anhydrothymidine (compound 4) to make compound 8, which (compound 8) is similar to the instantly claimed compounds except that the 5'-hydroxyl is not protected. But one of skill in the art will recognize that the same type of anhydrothymidine can be made by linking the enolate oxygen from the pyrimidine moiety to the 3'-position of the sugar ring. This is just an extension of the same chemistry with just the anhydro link being made to a different position. Fox need not explicitly suggest this. This will be recognized by one of ordinary skill in the art.

It is also true that the 2,5'-anhydrothymidine of Fox has a 7-membered ring whereas the 2,3'-anhydrothymidine of the instant invention has a 6-membered ring. The stabilities of the two rings systems and their reactivities may be different. It doesn't mean that the ring opening will not proceed at all in both cases. Difference in reactivity does not always equate to no reaction.

Not all reactions are unpredictable. If this is the case then many syntheses reported in the art would not have been possible. The advancement in synthesis is based also on applying known reactions to build new molecules. It is application of known chemistry used elsewhere in a particular step in the synthetic sequence at hand. That is how the art advances. Every step or reagent or starting material need not be specifically taught in the art. One of ordinary skill in the art can recognize it based on the teachings and one's own knowledge. In the instant case replacing the 2,5'-anhydrothymidine derivative of Fox with the 2,3'-anhydrothymidine derivative to arrive at the claimed invention will be recognized by one of skill in the art and he or she would have a reasonable expectation of success with both 7-membered and six membered rings.

The use of alkoxide as instantly claimed is a matter of choice since alkoxide is also a well known base used frequently in organic synthesis. The statement that the conversion of compound 4 to compound 8 as in Fox may not be feasible in alkoxide since the mesylate at the 3' position may also get cleaved is just an opinion. Applicants have not provided any supporting evidence. One of ordinary skill in the art will recognize that in the instant case the 5'-position has to be protected before the ring opening reaction of the anhydrothymidine since an alkoxide is used as a base for ring opening. If the 5'-position is left unprotected the alkoxide, which is a strong base, will abstract the hydrogen as a proton from the 5'-hydroxyl. In order to avoid this side reaction and direct the alkoxide as a nucleophile to open the ring the 5'-position has to be protected. Again this fact need not be taught or suggested by Fox or Miller. It will be recognized by the skilled artisan. Also, the fact that the 5'-position need not be protected in Fox et al since it is forming a cyclic ring is not relevant since Fox is forming a link to the 5'-position and needs a

leaving group there. Here again the use of reagents and modification of the steps depends on the end result desired. Compound 4 of Fox is similar to the starting material in instant step 1a except that there is no protected hydroxyl at the 5' position and the ring is formed at the 3' position in the instant case.

Compound 8 of Fox is similar to the product obtained in instant step 1b without the protecting group at the 3'-position. Since a methoxy is desired at the 2-position of the pyrimidine ring one of skill in the art will recognize that the ring opening should be performed with an alkoxide like methoxide, for example, in order to introduce the methoxy group at the 2-position of the pyrimidine ring. Or in other words, the amine (base) of Fox has to be substituted with methoxide as the base. This modification is well within the skill level of the artisan and also well within the artisan's skill level to recognize the modification. It need not be taught or suggested by Fox or Miller.

Based on the teachings of the prior art, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make compounds as claimed via the process as claimed since structurally very close compounds as instantly claimed and steps for the same are seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make compounds as instantly claimed via the process as instantly claimed and taught by the prior art, since they serve as intermediates for the syntheses of several other derivatives having biological activity including antitumor activity as taught by Fox and Miller. Similarity in structure and function entails motivation for making the compounds as instantly claimed via the method as instantly claimed.

The use of the process steps taught in the prior art with some modifications is well within the skill level of the artisan. Such is also routine in the art.

Obviousness based on similarity of structure and function entails motivation to make the claimed compound in expectation that compounds similar in structure will have similar properties. Where prior art compound essentially brackets the claimed compounds and are well known biologically active agents, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new agents. In re Payne, 606 F. 2d 303, 203, USPQ, 245, 254-55 (C.C.P.A. 1979).

Conclusion

Claims 1-5, 7-14, 16-22 and 25-31 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/

Examiner, Art Unit 1623

/Shaojia Anna Jiang/

Supervisory Patent Examiner, Art Unit 1623